AS Unit BY2: Biodiversity and Physiology of Body Systems

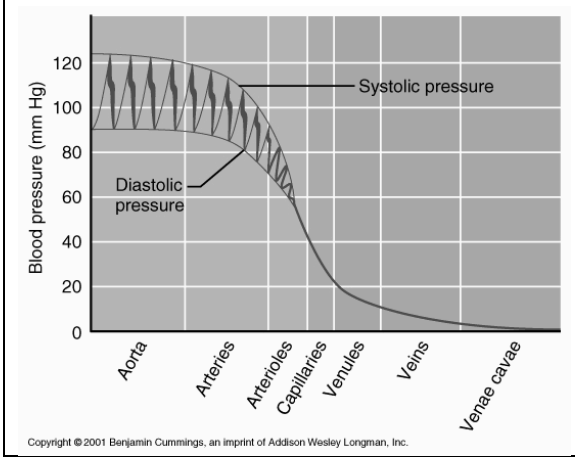
Name:	Date:

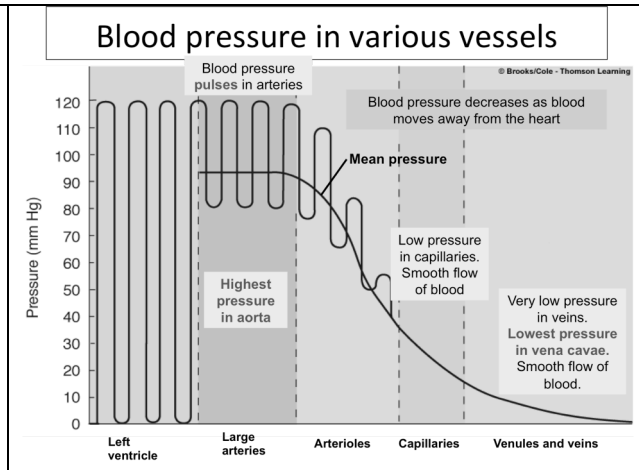
Topic 2.3 Transport (Animal) – Page 3

		Completed
1.	Read and discuss page 2 about blood pressure. Look carefully at the graphs and ensure that you can explain the reasons behind the drops in pressure. • Complete the questions on page 3.	
2.	Read page 4-5 about the formation of tissue fluid. • Complete the questions on the bottom of page 5 and the questions on page 6.	
3.	Read 7-8 about partial pressure and oxygen dissociation curves. • Complete the questions on 9-10	
4.	Extra Reading: Oxford Revision Guide Sheets BioFactsheets on Tissue Fluid and Partial Pressure Toole and Toole Understanding Biology p440-441, p414-419	

Blood Pressure and Flow

Look at the diagram on the right and at the changes of pressure in the left ventricle, label when you think the ventricle is in systole and when it is in diastole.





Changes in the pressure of blood of a reclining adult as it flows from the left ventricle through the circulatory systems and back to the heart via the vena cava are shown above.

Arteries

Blood leaves the ventricle in spurts, corresponding to the contractions of the ventricles.

When blood fills the aorta, the semi-lunar valves at the entrance prevent the back-flow of blood and the wall of the first part of the artery is distended (stretched). As the heart relaxes, the distended section recoils, which distends the next section – and so on.

This pulse wave of blood continues throughout the arteries and arterioles and, where an artery can be pressed against a bone, may be felt as your pulse.

As soon as blood leaves the left ventricle, there is **friction** between blood and the wall of the aorta.
This friction causes a drop in blood pressure; we say that there is **flow resistance**. The **velocity of blood flow is directly proportional to the pressure**.

Arterioles

Have a large total surface area and relatively narrow bore (lumen), this increases the flow resistance and blood pressure drops further. The pressure in arterioles can be altered by changing the diameter of the lumen using muscles found in the walls of the arterioles.

Capillaries

A large drop in pressure occurs when blood reaches the capillary beds. The millions of capillaries in the body form a large total internal surface area, which results in much friction. As well as friction a further drop in pressure occurs due to leakage of plasma during the formation of tissue fluid.

Veins

As a result of the drop in pressure across capillary beds, the pressure of blood in the veins is very low. Continued friction between the blood and walls of the veins reduces this pressure still further.
The pressure in the veins is so low that it is insufficient to return the blood to the heart. An increase in pressure, caused by exercising and contracting skeletal muscles pushing against the veins helps to push blood back to the heart. Semi-lunar valves help to prevent backflow. (The negative pressure developed in the thorax during inspiration will also help to draw blood back to the heart.)

Blood Pressure – Questions

The table below shows the minimum and maximum blood pressures in blood vessels.
A to F in the systemic circulation and in the aorta.

Blood vessel	Mean Blood Pressure (KPa)	
	Minimum	Maximum
Aorta	12	18
A	4	7
B	8	11
C	1	3
D	9	14
E	-2	0.5
F	10	16

Giving reasons identify which of the blood vessels A-F is:

i. the vena cava

ii a capillary

Which blood vessels A-F is likely to contain valves to prevent backflow?

The table below shows the mean diameter of some blood vessels and the mean velocity of blood travelling within these vessels.

Blood vessel	Mean diameter of vessel (mm)	Mean velocity of blood (cm s^{-1})
Aorta	10.0	40
Arteries	3.0	40-10
Arterioles	0.02	10-0.1
Capillaries	0.008	< 0.1
Venules	0.03	< 0.3
Veins	6.0	0.3-0.5
Vena cava	12.5	5-20

Describe the relationship between the diameter of the vessels and the velocity of the blood.

Explain the reasons for this relationship

The Formation of Tissue Fluids

Ringer's Solutions
If tissues are removed from the body and subjected to conditions different form those in the body, they will die.

Physiologist Sidney Ringer perfected the art of keeping tissues and organs alive outside the body. He found for example that the heart of a frog would continue to beat for some time outside the body if kept in a mixture of potassium, sodium and calcium salts and of course an adequate supply of oxygen.

It is now known that virtually all tissues can be kept alive in a suitable mixture of ions similar to the tissue fluids that bathe cells. These solutions are known as physiological saline's or Ringer's solutions. They have particular significance in transplant operations; organs that are transported from the donor to the recipient are bathed in Ringer's solutions.

How Tissue Fluid is formed

Tissue fluid is formed from the blood by a process of **ultrafiltration**. Analysis of tissue fluid shows that it is identical to blood plasma (note plasma does not have cells!) minus the blood proteins.

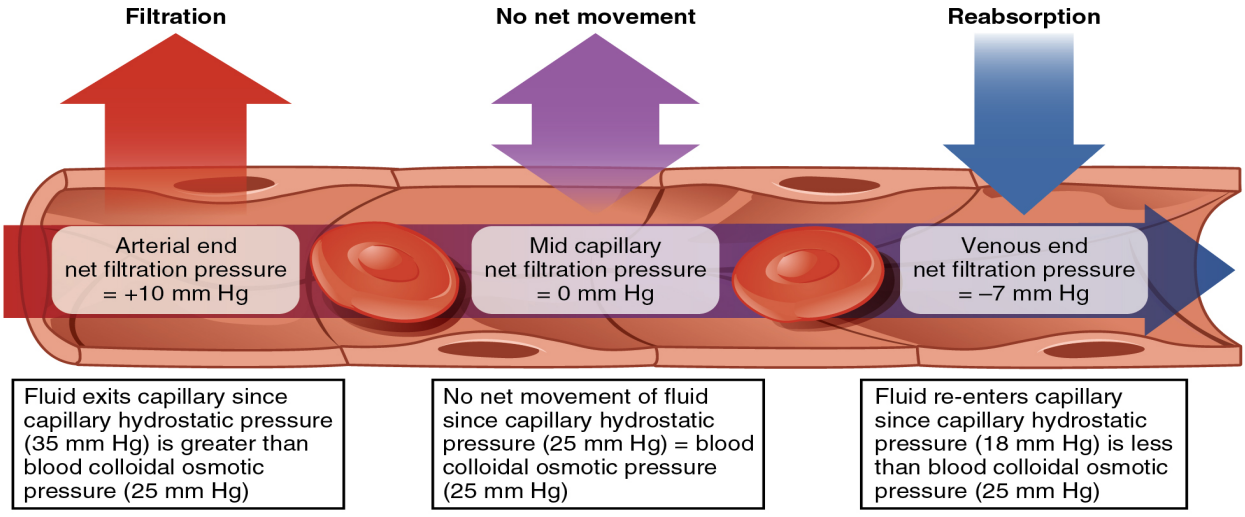
The walls of the capillaries, made from endothelial cells, are highly fenestrated (have many holes). Beyond the capillary walls is a basement membrane that acts as a selective filter preventing the passage of proteins and blood cells into the tissue.

The two pressures within capillaries are the hydrostatic pressure and the osmotic pressure.

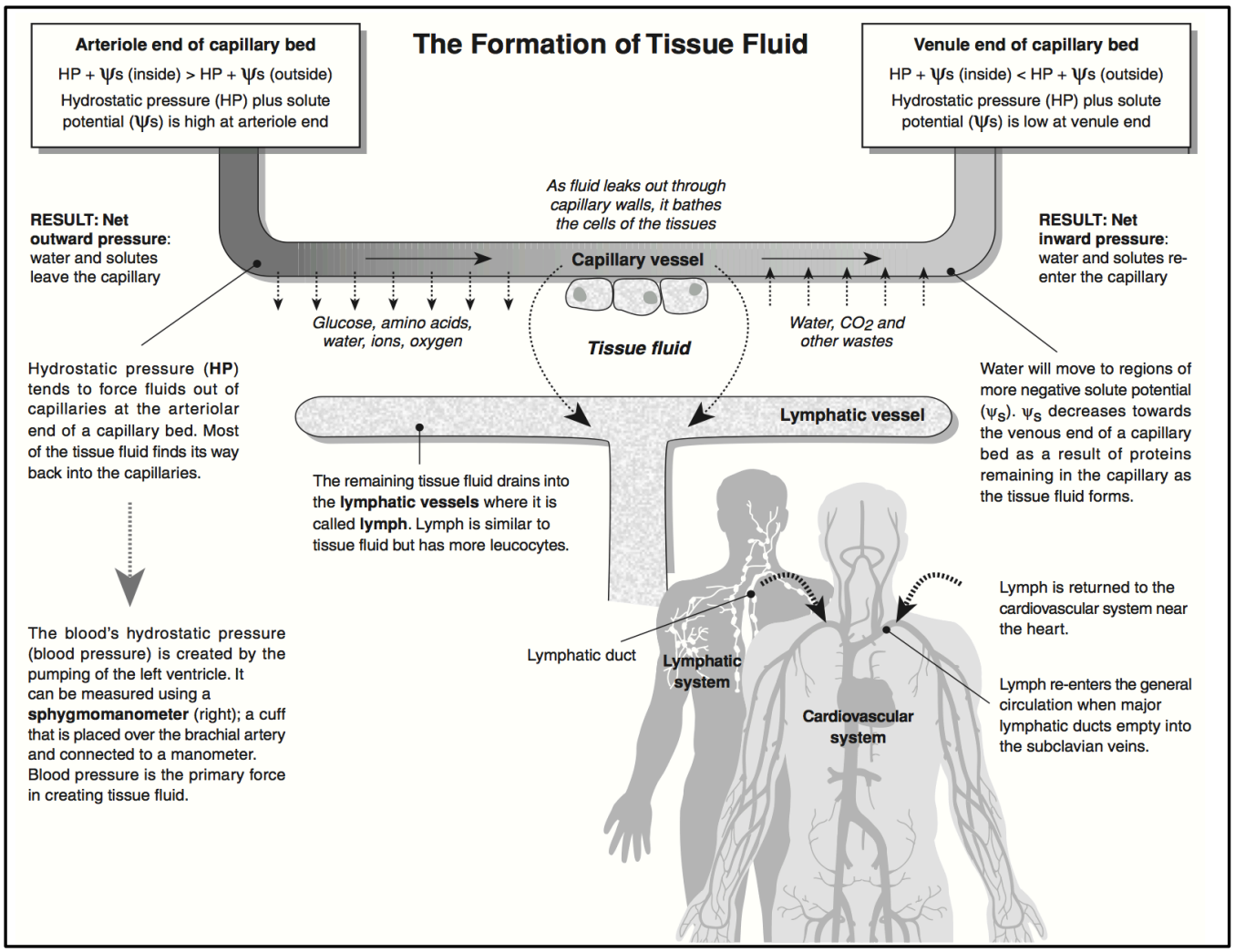
The **hydrostatic pressure** (force exerted by the blood against the walls of the vessels) is caused by the caused by the contraction of the ventricles of the heart. This pressure will tend to force water, ions and small molecules out of the capillary.

O**smotic pressure** is due to the presence of plasma proteins, this pressure tends to pull water into the capillary.

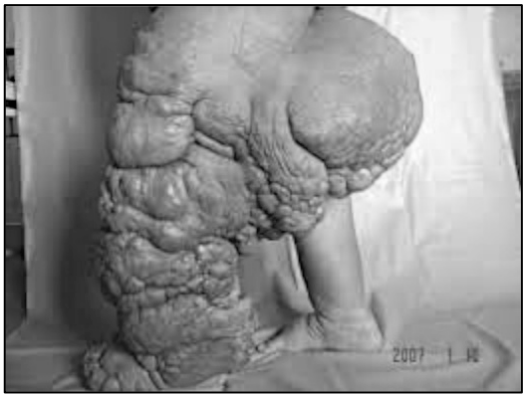
At the arteriole end hydrostatic pressure is greater than the osmotic pressure and water, ions and small molecules are forced through the capillary wall into the tissue fluid.
The movement of fluid out of the capillary causes the hydrostatic pressure within the capillary to fall and at the venule end of the capillary the osmotic pressure is greater than the hydrostatic pressure. This causes water and solutes will move back into the capillary. (in addition to this the venous ends of the capillaries have low hydrostatic pressure due to the capillaries opening into much wider venules)



In an average human, about 3dm^3 more fluid leaves the capillaries as tissue fluid each day than is reabsorbed at the venule end of the capillaries. If this fluid were allowed to remain and accumulate it would cause, the tissues to swell, a condition known as **oedema**. Blind-ended capillaries of the lymph system normally collect the tissue fluid that does not move back into the venous ends of the capillaries.



The lymphatic system relies on skeletal muscular contractions to massage and push the fluid back to the subclavian valve, near the heart where it renters the bloodstream.

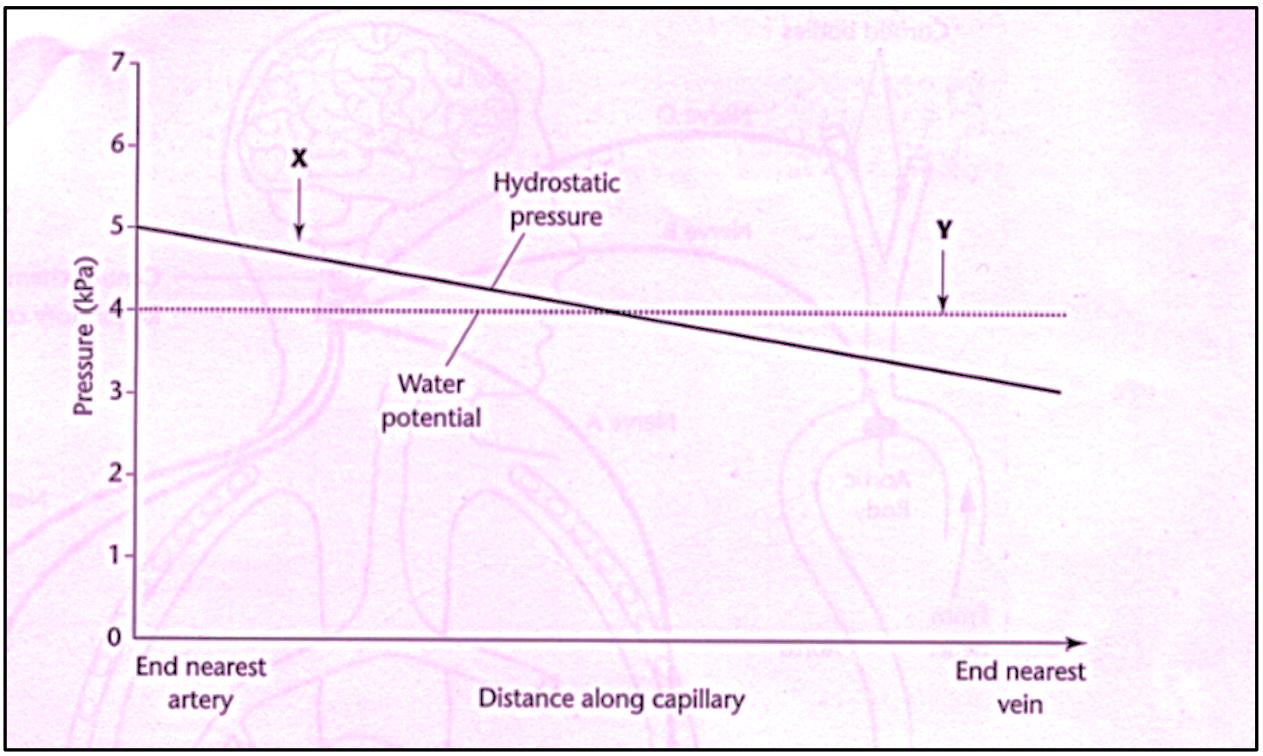


Oedema may be result from the following clinical disorders:

- excessively high blood pressure
- a protein-deficient diet
- a blockage of lymph vessels by a parasitic worm (elephantitis).

In each case, explain why the oedema occurs.

Questions on the Formation of Tissue Fluid



1.What causes hydrostatic pressure in the blood?

2. Which component of the plasma decreases the water potential of the blood by the greatest amount?

3. Explain why there is a net movement of fluid into the tissues at point X on the graph.

4. Describe how materials re-enter the blood at point Y on the graph.

5. A parasite which lives in tissue fluid can block lymph capillaries, causing swelling of the tissues, particularly in the leg. Explain why blockage of the lymph capillaries leads to swelling of the tissues.

6. List the substances that blood transports in addition to oxygen and carbon dioxide.

Transport of Gases

Partial Pressure
The oxygen content of the air is measured as a partial pressure. The partial pressure of a gas is a measure of its concentration and is expressed in kilopascals (KPa). For example, at sea level the total atmospheric pressure is 101.3KPa and because the atmosphere contains about 21% Oxygen, this gas contributes about 21% of the total pressure, which 21.2KPa. In other words, the partial pressure of oxygen is a measure of how much of the pressure exerted by a mixture of gases can be attributed to oxygen.

The transport of respiratory gases around the body is the role of the blood and its respiratory pigments. Oxygen is transported throughout the body chemically bound to the respiratory pigment, haemoglobin.

Oxygen Dissociation Curves
Haemoglobins are the most common oxygen carrying pigment. They are made up of two parts; a prosthetic group and a protein. The protein part consists of four polypeptide chains known as globin, each associated with a complex iron containing prosthetic group called **haem**.

Red blood cells contain the pigment haemoglobin, a compound which combines easily with oxygen. A single haemoglobin molecule can bind up to four oxygen molecules.

$$Hb + 4O_2 \underset{\text{in tissues}}{\overset{\text{in lungs}}{\rightleftharpoons}} HbO_8$$

haemoglobin oxygen oxyhaemoglobin

In the alveoli of the lungs, blood travelling through the pulmonary capillaries picks up (loads) oxygen. The **partial pressure of oxygen (**or **oxygen tension**) in the alveoli is relatively high, and under these conditions haemoglobin will become saturated with oxygen. The blood then carries the oxygen round the body to respiring cells, where the partial pressure of oxygen is low. Under these conditions, oxyhaemoglobin gives up its (unloads) oxygen, or dissociates, and the oxygen diffuses into the respiring cells.

An oxygen dissociation curve always has an S-shape (Fig.1). This is because the first oxygen molecule has some difficulty in combining with an iron atom in a haemoglobin molecule. But the presence of this first oxygen molecule distorts the shape of the haemoglobin protein, making it easier for the remaining three molecules to combine with the iron atoms.

Fig. 1 Oxygen dissociation curve

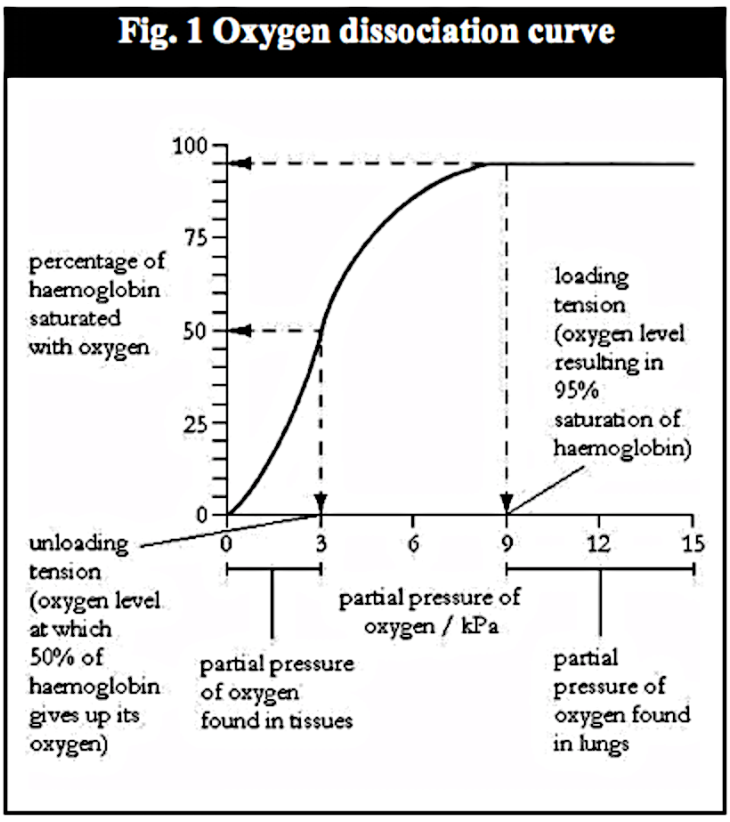
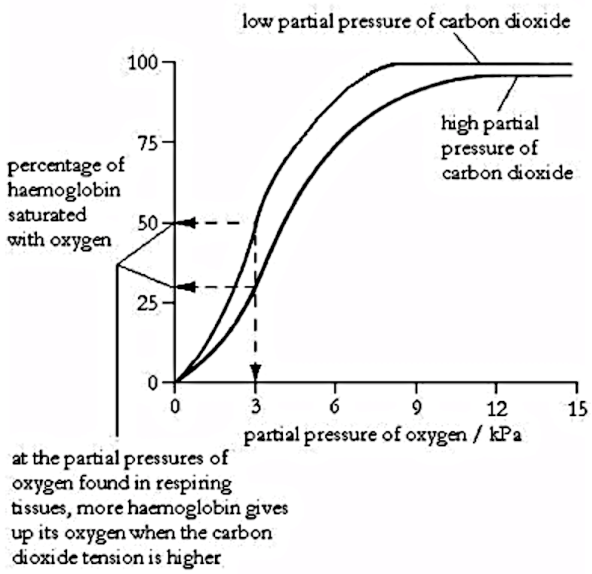


Fig. 2 The Bohr shift



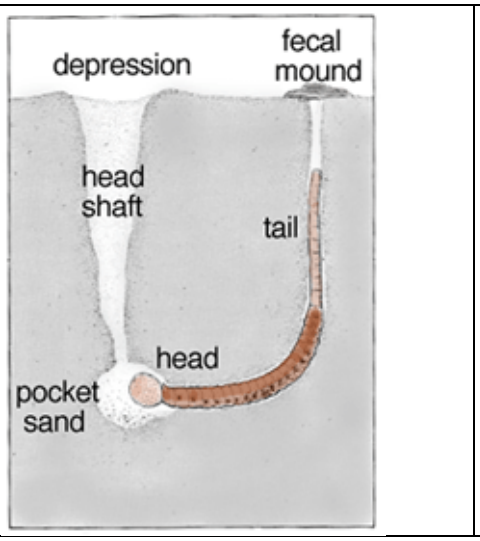
at the partial pressures of oxygen found in respiring tissues, more haemoglobin gives up its oxygen when the carbon dioxide tension is higher

In respiring cells, a rise in the partial pressure of carbon dioxide increases the rate of dissociation of oxyhaemoglobin. This has the effect of moving the oxygen dissociation curve to the right, a phenomenon known as the Bohr shift (Fig. 2). A rise in temperature also has the same effect. In this way, oxyhaemoglobin releases more oxygen where it is most needed – in the most actively respiring tissues.

Can you suggest a mechanism to explain the affinity of haemoglobin may change with an increase in carbon dioxide concentration?

There a certain types of blood pigment which can readily take up oxygen even when the partial pressure of oxygen is very low.

Myoglobin is found in skeletal muscle. Myoglobin stores oxygen, releasing it when the partial pressure of oxygen falls very low, as in severe muscle exertion. Myoglobin is responsible for the colour of red muscles and is particularly abundant in animals that are either very active or diving mammals such as seals. Interestingly the haemoglobin of lugworms, which burrow in oxygen deficient mud, is functionally very similar to myoglobin. The oxygen dissociation curve for lugworm haemoglobin lies to the left of that for human haemoglobin and reflects it high affinity for oxygen even at low partial pressures.



As well as haemoglobin of different species varying in their affinity for oxygen, it may even change during the life cycle of a single individual. For example, foetal haemoglobin has an oxygen dissociation curve situated to the left of human adult haemoglobin. Foetal blood has to be able to pick up oxygen from maternal blood across the placenta and this can only take place if the foetal blood has a higher affinity for oxygen.

Task

Varying the carbon dioxide levels

Table 2 shows the results of an investigation into the relationship between oxygen partial pressure and the percentage saturation of the blood with oxygen at two different concentrations of carbon dioxide. This represents the conditions found in tissues respiring at different rates.

Table 2. Oxygen dissociation at different partial pressures of CO_2

	% saturation of blood with oxygen	
Partial pressure of O_2 (kPa)	3 kPa CO_2	11 kPa CO_2
0	0	0
1.3	10	5
2.7	22	12
4.0	60	24
5.3	84	42
8.0	94	78
10.7	97	90
13.3	98	95

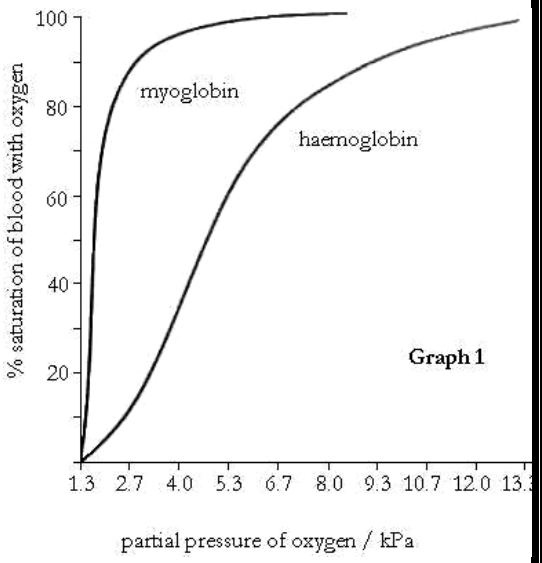
3.
   a. Plot the results on a graph, with oxygen partial pressure on the horizontal axis.
   b. Describe the effect that carbon dioxide has on the oxygen haemoglobin dissociation curve.
   c. What tissues of the body would you expect to have higher carbon dioxide partial pressures than blood?
   d. Explain how a shift in the oxygen haemoglobin dissociation curve can allow actively respiring tissues to acquire greater amounts of oxygen.

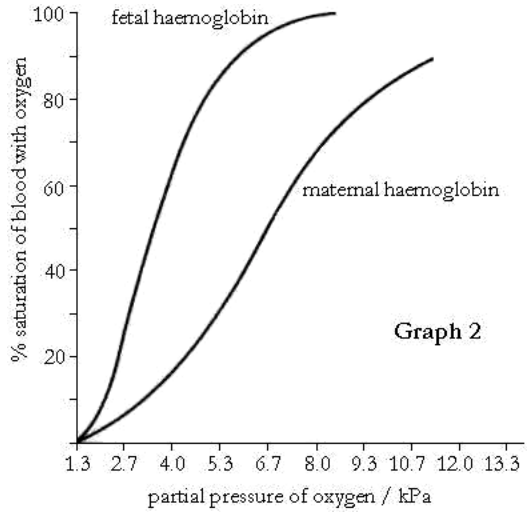
Factors affecting oxygen dissociation

As the carbon dioxide partial pressure of the tissues and capillary blood rises, the affinity of oxyhaemoglobin for oxygen is lowered. The phenomenon is called the Bohr effect, after the scientists who first recorded it. The oxygen dissociation curve moves to the right.

Study Graphs 1 and 2 and then answer the questions.

4. Look at the Graph 1.
   a. Which respiratory pigment has a greater affinity for oxygen?
   b. In which tissue of the body will you find myoglobin?
   c. Can you suggest what use myoglobin may have if the oxygen content of exercising muscle is near zero?

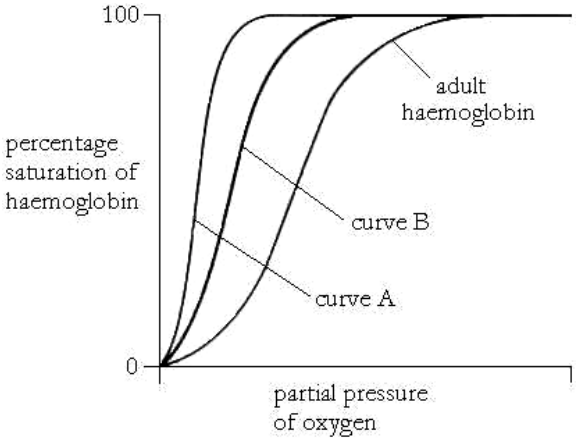




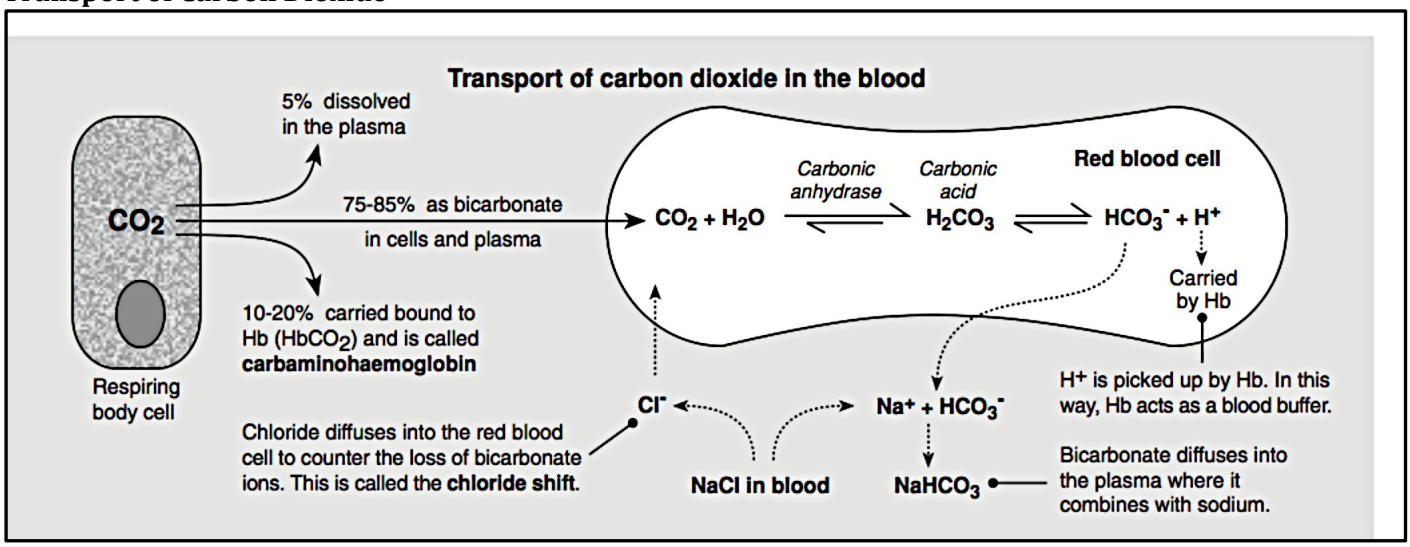
5. Look at Graph 2.
   a. At what partial pressure of oxygen is the oxygen saturation of 50%:
      In the mother;
      In the fetus?
   b. How does the difference in the oxygen loading between maternal and fetal blood help the transfer of oxygen from the mother to the fetus?

6.
   a. What is meant by the partial pressure of oxygen?
   b. Explain why the curve for adult human haemoglobin is S-shaped.
   c. What happens to the partial pressure of carbon dioxide in a muscle when it is undergoing exercise?
   d. Explain how your answer to (c) could result in exercise leading to more oxygen being supplied to the muscle.

6. Various animals have haemoglobin that has a dissociation curve with the same shape as curve B.
   a. How would the loading tension of this type of haemoglobin differ from that of human haemoglobin?
   b. Explain the advantage of haemoglobin of this type in places where the amount of oxygen is low.
   c. Explain why the following might be expected to have this type of haemoglobin:
      a human fetus in the uterus of its mother;
      a llama living at high altitude in the Andes;
      a carp living in deep water with large amounts of rotting vegetation.



Transport of Carbon Dioxide



Carbon dioxide diffuses from the tissues into the red blood cells where it combines with water to form carbonic acid, H_2CO_3. This is normally a very slow reaction, but in the red blood cell it is greatly accelerated by the presence of an enzyme called carbonic anhydrase. Due to this enzyme most of the carbon dioxide enters the red blood cells rather than remaining in the plasma.

The carbonic acid dissociates into hydrogencarbonate and hydrogen ions.

The hydrogen ions if allowed to accumulate, lower the pH of the red blood cell and could kill the cell. The haemoglobin buffers the hydrogen ions, oxyhaemoglobin dissociates from the oxygen and takes up the hydrogen ions to form haemoglobinic acid.

(NOTE the Bohr shift is not directly due to the presence of carbon dioxide itself but from the H^+ resulting from its presence)

The hydrogencarbonate ions that accumulate readily diffuse out of the red blood cell. To maintain electroneutrality (from the H^+) chloride ions diffuse in from the blood plasma, this is called the **chloride shift**.

Bio Factsheet

Number 89

Tissue Fluid

After studying this Factsheet the student should know and understand:

- **the nature of tissue fluid and lymph**
- **the functions of tissue fluid**
- **the formation and drainage of tissue fluid**
- **the cause of oedema**

As cells become more differentiated and specialised, the less capable they are of surviving independently. They are less able to protect themselves from toxic chemicals, pH changes or extreme temperatures and, if fixed in position within a tissue, cannot seek food, ingest solid bits of food or move away from their own toxic products. The substance that bathes cells and performs these vital functions for them is called **tissue fluid** (or **interstitial fluid** or **intercellular fluid**).

***Remember**- do not confuse intercellular fluid and extracellular fluid. **Extracellular fluids** are all fluids outside the cells including blood plasma, tissue fluid, lymph, cerebro-spinal fluid, synovial (joint) fluid and the aqueous humour of the eye. The term **intercellular fluid** refers to tissue fluid only. Do not confuse either of these terms with intracelluar fluid - the fluid inside cells.*

The tissue fluid is 'serviced' by the blood and lymph in the following ways:

- the blood transports oxygen, nutrients and hormones to the tissues where they move out of the capillaries (at the arterial end) into the tissue fluid. The mechanisms of movement involved include osmosis, diffusion and filtration. These substances are passed into the cells and the cells pass wastes into the tissue fluid.
- a large proportion of the waste materials pass from the tissue fluid back into the blood in the capillaries (at the venous end).
- the remaining waste products pass into the lymph in the lymph vessels. The lymph is returned to the blood stream (where the main lymph vessels join the subclavian veins).

The difference in protein content between the blood plasma and the tissue fluid is because protein molecules are too large to pass through the capillary membranes and so are retained in the blood. This is important since these proteins help to maintain the osmotic pressure of blood.

The lymph nodes, which are situated in lymph vessels, store and manufacture lymphocytes which are released to the lymph. Lymphocytes are 'immunity' cells which secrete antibodies and other 'cytotoxic' substances. Other white blood cells, such as the phagocytic neutrophils, escape through the capillary walls to the tissue fluid by the process called diapedesis (the cells push between the capillary wall cells using their pseudopodia).
Bacteria in the tissues, tissue fluid and lymph can be destroyed in the following ways:

- by phagocytosis by neutrophils present in the tissue fluid and lymph.
- by phagocytosis by macrophages in the lymph nodes through which the lymph is filtered.
- by antibodies and cytotoxins secreted by the lymphocytes.

***Remember** – capillary walls are lined by a very thin pavement epithelium and its basement membrane of fine connective tissue fibres. In places, called fenestrations, the cells are missing and only the basement membrane is present. It is mainly the basement membrane that acts as a 'molecular sieve' preventing protein loss from blood.*

Production and drainage of tissue fluid

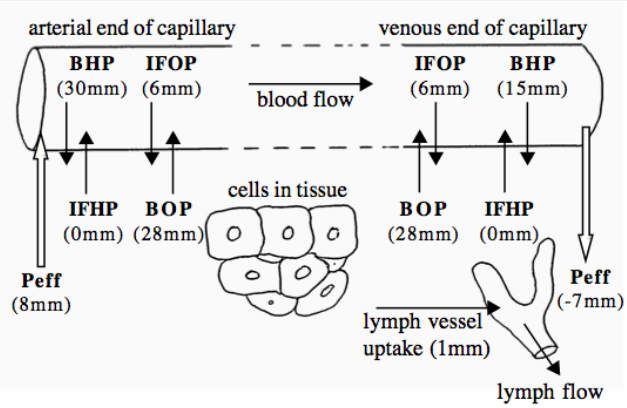
The movement of water and dissolved substances (except proteins) through capillary walls occurs by diffusion and filtration but is dependent on various opposing hydrostatic forces or pressures. Some pressures force fluid out of capillaries into the surrounding tissue spaces and this results in filtration of the fluid. So that fluid does not remain in the tissue spaces and accumulate, opposing pressures force fluid from the tissues spaces back into the blood capillaries and this results in reabsorption of fluid. Any fluid not reabsorbed into the capillaries is returned to the blood as lymph, via the lymphatic vessels.

Table 1. The main differences between blood plasma, tissue fluid & lymph

	blood plasma	tissue fluid	lymph
position	in arteries, capillaries and veins.	between cells in tissues.	in lymph vessels, which have the same structure as veins.
protein content	high	very low	very low
oxygen and nutrient content	high	high (arterial end) low (venous end)	low
waste content	low (since constantly removed via kidneys)	low (arterial end) high (venous end)	high
cell content	carries many red blood cells and white blood cells in approximate ratio red:white of 1000:1	contains many white cells which escape from blood, (e.g. neutrophils)	contains same white cells as tissue fluid plus lymphocytes made in the lymph nodes.

The production and drainage of tissue fluid is illustrated in Fig 1 and explained in the text below the diagram.

Fig 1. The production and drainage of tissue fluid



Key: BHP = blood hydrostatic pressure
BOP = blood osmotic pressure
IFHP = interstitial fluid hydrostatic pressure
IFOP = interstitial fluid osmotic pressure
Peff = effective filtration pressure

Four basic pressures are involved in tissue fluid formation and drainage. These are:

- **blood hydrostatic pressure (BHP)** This blood pressure tends to force fluids out of capillaries into the tissue fluid. BHP averages about 30 mm of mercury at the arterial end of the capillary bed and about 15 mm of mercury at the venous end. This fluid carries out oxygen, sugars, amino acids, salts, vitamins and some hormones from the blood plasma to the tissue fluid. However, proteins which have a large molecular size cannot escape through the differentially permeable capillary membranes and so remain in the blood. This filtration means that tissue fluid contains only a small quantity of protein.

- **interstitial fluid hydrostatic pressure (IFHP)** This tissue fluid pressure tends to move fluid from the tissues back into the blood. Its value is generally very small and can vary from positive to negative values. (In the calculations below we shall use a value of 0 mm of mercury at both ends of the capillary bed).

- **blood osmotic pressure (BOP)** This pressure generally has a value of about 28 mm of mercury at both arterial and venous ends of the capillary bed. The pressure arises mainly from the high concentration of non-diffusible plasma proteins in the blood. The BOP tends to move fluid from the tissue fluid back into the capillaries.

- **interstitial fluid osmotic pressure (IFOP)** This pressure generally has a value of about 6 mm of mercury at both ends of the capillary bed. It arises due to the presence of small quantities of protein within the tissue fluid. Only minute quantities of protein leak from capillaries into the tissue fluid, but proteins such as enzymes and some hormones may actually be secreted into the tissue fluid by cells. This pressure tends to move fluid from capillaries into the tissue fluid.

Whether fluid moves in or out of capillaries depends on how the pressures interact together. If the forces moving fluid out of capillaries are greater than the forces moving fluid into capillaries then the production of tissue fluid (filtration) will occur. This happens at the arterial end of capillaries. If the forces moving fluid into capillaries are greater than the forces moving fluid out of capillaries then tissue fluid will tend to be drained back to the blood (reabsorption). This happens at the venous end of capillaries.

The term **effective filtration pressure (Peff)** is used to show the direction of fluid movement. It can be calculated by the equation:

Peff = forces moving fluid out of capillaries – forces moving fluid into capillaries

Thus Peff = (BHP + IFOP) – (IFHP + BOP)

Thus at the arterial ends of the capillary bed
Peff = (30 + 6) – (0 + 28) = 8 mms of mercury.
This net outward force moves fluid out of the capillaries to form tissue fluid.

At the venous end of the capillary bed
Peff = (15 + 6) – (0 + 28) = -7 mms of mercury.
This net inward force tends to draw fluid back into the capillaries.

The net inward force is less than the net outward force (by 1 mm of mercury) and so not all the tissue fluid formed can drain back to the capillaries. The remainder is forced into the lymph vessels to be returned as lymph to the blood, via the lymph drainage system.

Exam hint *– examiners will not expect you to remember the actual values for the different pressures but you need to know whether they are large or small so that you can show how they relate together in tissue fluid circulation. Questions may be asked as data interpretation exercises.*

Oedema and its causes

Oedema is the accumulation of fluid within the tissues and is due to an imbalance of filtration and reabsorption between tissue fluid and plasma. It usually appears first at the ankles which become swollen with fluid. The following are some of the possible causes:

- raised blood hydrostatic pressure (BHP) in capillaries due to an increase in venous pressure. This could be due to obstruction of venous return due to cardiac inefficiency or to blood clots blocking the veins.

- decreased plasma proteins that lower blood osmotic pressure (BOP). Blood protein may be lost due to liver disease, kidney disease, malnutrition or from burns.

- increased capillary membrane permeability will raise interstitial fluid osmotic pressure (IFOP) by letting considerable quantities of plasma proteins leak from the blood into the tissue fluid. Increases in capillary permeability can result from bacterial or viral infection or be caused by chemical, thermal or mechanical agents (eg. bruising).

- increased extracellular fluid volume as a result of fluid retention. In kidney inefficiency the person may not be capable of voiding large volumes of water but still drinks a normal volume. This extra water tends to raise the blood plasma volume and thus raises the blood hydrostatic pressure (BHP).

Exam hint *– questions relating to oedema are more likely to occur in examinations testing units about Health and Disease.*

Practice Questions

Remember *– recommended units for measuring pressure are now the* ***pascal (Pa)*** *or* ***kilopascal (kPa)****. In physiology and medical practice the units 'mms of mercury' are still commonly used, simply because nearly all the instruments used for measuring pressures are calibrated in 'mms of mercury' and it would cost vast sums of money to replace them., Also, having two types of unit in use could result in serious medical errors occuring.*
1mm of mercury = 133.3 Pa.
BHP = 3999 Pa. IFOP = 799.8 Pa. BOP = 3732.4 Pa.
Data interpretation questions may use mms of mercury or pascals.

1. (a) State **two** features of capillaries that enable tissue fluid to be formed. 2

   (b) About 85% of the tissue fluid is reabsorbed at the venous end of the capillary. Describe what happens to the tissue fluid that is not reabsorbed. 3

   (c) List **three** differences in the composition of tissue fluid at the arterial end of the capillaries to the tissue fluid at the venous end of the capillaries. 3

   (d) When tissue fluid is inadequately reabsorbed, it accumulates in the tissues causing swelling (oedema). Suggest **two** possible causes for oedema. 2

   Total 10

2. (a) Distinguish between:
   (i) tissue fluid and lymph, 1
   (ii) tissue fluid and plasma, 2
   (iii) extracellular fluid and intercellular fluid. 2

   (b) The equation below for effective filtration pressure relates the different pressures involved in forming tissue fluid. The table gives some actual values for some of these pressures and also some normal values bracketed in italics.

   Peff = forces moving fluid out of capillaries − forces moving fluid into capillaries

   Thus Peff = (BHP + IFOP) – (IFHP + BOP)

pressures in mm of mercury	**arterial end of capillary bed**	**venous end of capillary bed**
blood hydrostatic pressure (BHP)	**?**	16 *(15)*
interstitial fluid osmotic pressure (IFOP)	6	6
interstitial fluid hydrostatic pressure (IFHP)	0	-1*(0)*
blood osmotic pressure(BOP)	28	28
effective filtration pressure (Peff)	10 *(8)*	**?** *(-7)*

   (i) Use the equation to calculate the missing values on the table. Show your working. Only use the actual values. 4
   (ii) Comment on the values shown in the table. 3

   Total 12

Answers

1. (a) ref to very thin pavement epithelium (of wall);
   ref to fenestrations/cell gaps in wall;
   ref to differentially permeable capillary walls (so that proteins cannot cross it); max 2

   (b) taken up into lymph vessels (as lymph);
   aided by a positive tissue fluid hydrostatic pressure/pressure of 1 mm of mercury;
   returned to blood system (at subclavian veins)
   bacteria filtered out of lymph by phagocytes in lymph nodes;
   lymph nodes release lymphocytes into the lymph; max 3

   (c) arterial end contains higher concentration of oxygen than venous end;
   arterial end contains a higher concentration of glucose/amino acids/ any correct named nutrient than venous end;
   arterial end contains a lower concentration of waste products/ correct named product than venous end; (only allow urea if liver is specified) 3

   (d) raised blood hydrostatic pressure/possible causes of this;
   decreased plasma protein concentration/possible causes of this;
   raised capillary wall permeability/possible causes of this;
   fluid retention/possible causes of this; max 2

   Total 10

2. (a) (i) tissue fluid is present between cells/in tissues but lymph is within the lymph vessels;
   lymph tends to contain more lymphocytes than tissue fluid; max 1

   (ii) tissue fluid contains very little protein but plasma contains a lot;
   tissue fluid is between the cells/in tissues but plasma is within the blood vessels;
   tissue fluid does not contain red cells but plasma does; max 2

   (iii) extracellular refers to all body fluids outside cells;
   intercellular fluid refers only to tissue fluid between the cells;
   blood plasma/lymph/tissue fluid/cerebrospinal fluid/synovial fluid/aqueous humour are all examples of extracellular fluid;
   (look for two examples for one mark) max 2

   (b) (i) Peff = (BHP + IFOP) – (IFHP + BOP)
   10 = (BHP + 6) – (0 + 28) ;
   BHP = 32 mm ;
   Peff = (16 + 6) – (-1 + 28) ;
   Peff = - 5 mm; 4

   (ii) the effective filtration pressure forming tissue fluid is higher than the norm;
   the effective filtration pressure reabsorbing tissue fluid is less than the norm;
   thus oedema may occur/tissue fluid may accumulate between cells; 3

   Total 12

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Bio Factsheet

Number 9

Oxygen Dissociation Curves

This Factsheet summarises:

1. **The mechanisms of oxygen and carbon dioxide transport in blood**
2. **The interactions between the mechanisms of oxygen and carbon dioxide transport and blood pH control.**
3. **The effects of factors such as temperature, pH, birth, body size and disease on oxygen dissociation curves.**

Examination questions on this topic usually test recall and understanding by providing data for comment and analysis. A detailed knowledge of haemoglobin structure is not required.

Transport of Oxygen

The respiratory pigment **haemoglobin** enables the blood to carry enough oxygen for the body's needs. The solubility of oxygen in the water of the plasma is low and decreases even further as the temperature rises. Thus the quantity of oxygen that could be carried by the plasma alone is not enough. The extra carriage of oxygen depends on the fact that one molecule of haemoglobin can **onload** four molecules of oxygen, one on each of the four haem groups of the pigment.

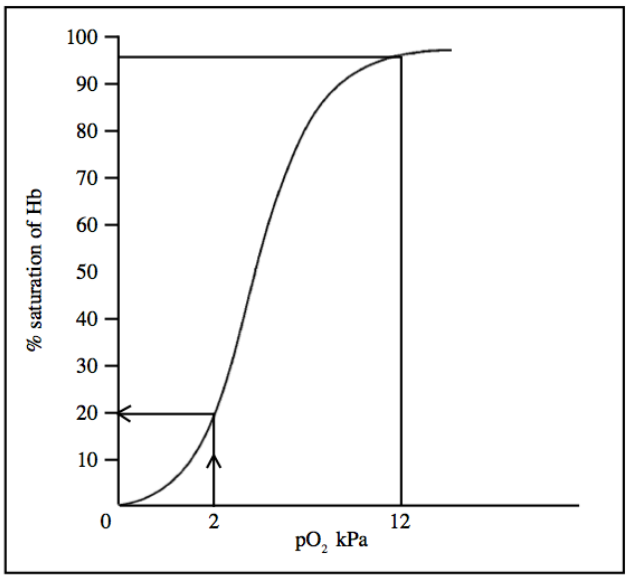
Inhaled alveolar air has an oxygen tension around 14kPa (kilopascals) whereas the oxygen tension in the blood supplying the lungs is between 2.7 and 5.3kPa. (This range depends on the oxygen tension of the tissues the blood has just left; 5.3kPa is the tension for resting tissues which are using little oxygen and 2.7kPa is for active tissues which are using much oxygen). Thus, there is a diffusion gradient across the alveolar surface (e.g. 14kPa - 5.3kPa = 8.7kPa) and so oxygen will diffuse from the alveolar surface into the blood and into the red blood cells. Once inside the red blood cells the oxygen is **onloaded** onto the haemoglobin until it is about 96% saturated. It is now called **oxyhaemoglobin**. The equation for this association of oxygen with haemoglobin is:

$$Hb + 4O_2 \rightarrow HbO_8$$

Fig 1. shows the percentage saturation of haemoglobin as it passes through areas of the body which have very different partial pressures of oxygen. At 2kPa of oxygen - i.e. at the very low partial pressures of oxygen which we would expect in actively respiring muscles, the percentage saturation of haemoglobin is very low (it is only 20% saturated; the other 76% has been released to the muscles through which the blood is flowing).
At 12kPa - i.e. at the very high partial pressures of oxygen found in the lungs - the haemoglobin is 96% saturated.

So, imagine a red blood cell in a capillary. As it passes through capillaries in the lungs, where the partial pressure of oxygen is very high (12-14kPa) it will **onload** oxygen i.e. pick up 8 oxygen atoms and become 96% saturated. The red blood cell then goes to the heart from where it is pumped out to the left leg of a marathon runner. The muscle is working hard i.e. respiring and using up a lot of oxygen. The partial pressure of oxygen in the muscle tissues is therefore very low (eg. 2kPa). As the red blood cell enters the capillaries within the muscle it finds itself in a region of very low partial pressures of oxygen and the haemoglobin therefore loses 76% of its oxygen. In other words, it releases 76% to the muscles and ends up only 20% saturated (see Fig 1). The muscle cells will use this oxygen to maintain aerobic respiration which thus provides a good supply of ATP so that it can carry on contracting and so that the athlete can carry on running (see Factsheet 12: Respiration).

Fig 1. Oxygen dissociation curve for haemoglobin



Why is the oxygen dissociation curve (ODC) S shaped ?
Each haemoglobin molecule can combine with a total of 4 O_2 molecules (one O_2 molecule for each of the haem groups).

1. The first O_2 molecule combines relatively slowly with the first haem group. Thus, the first part of the ODC is not very steep. However, the binding of oxygen with the first haem group causes the shape of the whole haemoglobin molecule to change.
2. As a result of its altered shape, it is much easier for the second and third O_2 molecules to bind to their haem groups. Thus, the ODC becomes much steeper.
3. The curve flattens off because it then becomes harder for the fourth (i.e. the last) oxygen molecule to combine with the fourth haem group.

Exam Hint *- Candidates frequently confuse oxygen pressure with blood pressure. Oxygen pressure, oxygen partial pressure and oxygen tension can be regarded as essentially the same thing - they are simply a measure of the concentration of oxygen in the blood.*

Exam Hint *- This is a favourite synoptic topic because it links molecular biology, biochemistry, physiology and adaptation.*

The effect of pH

The quantity of oxygen carried by haemoglobin depends on pH as well as on oxygen tension. In a more acidic environment oxygen dissociates from the haemoglobin more readily, whereas in a more alkaline environment association of oxygen with haemoglobin is favoured, forming more oxyhaemoglobin. This results in the **Bohr effect** which is illustrated in Figure 2.

For example, imagine the blood is flowing through capillaries where the surrounding tissues have an oxygen tension of 4 kPa:

At pH7.6 the Hb would be 74% saturated
But at pH 7.4 the Hb would be 59% saturated

In other words, as pH decreases (becomes more acidic) the haemoglobin has become less saturated - it has given some of its oxygen to the tissues.

At pH7.2 (even more acidic conditions) the haemoglobin is only 36% saturated i.e. it has released even more oxygen to the tissues. So as a general rule, as pH decreases (as conditions become more acidic) haemoglobin becomes less saturated and gives up more oxygen. Acidity can be defined as the concentration of hydrogen ions. Hydrogen ions can reduce haemoglobin by attaching to the same sites as oxygen atoms and thus they compete with oxygen for these sites. In an acidic environment the higher concentration of hydrogen ions displaces oxygen from haemoglobin and thus improves oxygen release into the tissues.

$$\underset{\text{oxyhaemoglobin}}{HbO_2} + H^+ \rightarrow \underset{\text{reduced haemoglobin}}{HHb} + O_2$$

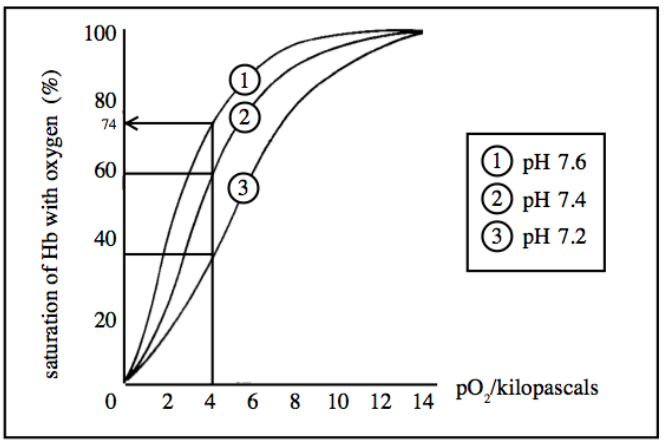
This is perfect because respiring tissues are acidic as a result of the carbon dioxide and/or lactic acid produced in respiration. Carbon dioxide dissolves to form carbonic acid and this stimulates the release of oxygen from haemoglobin, thus allowing the tissues to keep respiring aerobically.

The environment in the alveoli is less acidic (due to the lowering of carbon dioxide tension) and thus oxygen atoms predominate and tend to displace the hydrogen from the haemoglobin. This enhances the uptake of oxygen.

In this way the haemoglobin is acting as a **buffer**, limiting the range of blood pH between 7.2 and 7.6. This is an example of homeostasis, in this case keeping the blood pH within optimum range.

From Figure 2 it can be seen that: As pH decreases, the ODC moves to the right. This is called the **Bohr Effect**.

Figure 2. The effect of pH on the ODC (The Bohr Effect)



Transport of carbon dioxide

Carbon dioxide is released by respiring cells and diffuses into the blood plasma. About 5% of it dissolves directly and is carried in solution. The rest diffuses into the red blood cells where about 25% of it attaches onto the amino acid side chains of the protein globin in haemoglobin, forming **carbaminohaemoglobin**. (This is still able to carry oxygen or hydrogen on its haem groups.) The remaining 70% of the carbon dioxide enters red blood cells and is converted by the enzyme **carbonic anhydrase** to carbonic acid. This dissociates at once to form hydrogen ions and hydrogen carbonate ions.

$$CO_2 + H_2O \xrightarrow[\text{carbonic anhydrase}]{} \underset{\text{carbonic acid}}{H_2CO_3} \rightarrow H^+ + HCO_3^-$$

The hydrogen ions would decrease the pH of the blood if they remained free but they attach to the haem groups, displacing the oxygen into the tissues whilst limiting the pH change to pH 7.2. The hydrogencarbonate ions diffuse out of the red cells into the plasma, thus leaving a shortage of negative ions in the red cells. To compensate for this, chloride ions (Cl^-) move from the plasma into the red cells to restore the electrical balance. This is known as the **chloride shift**.

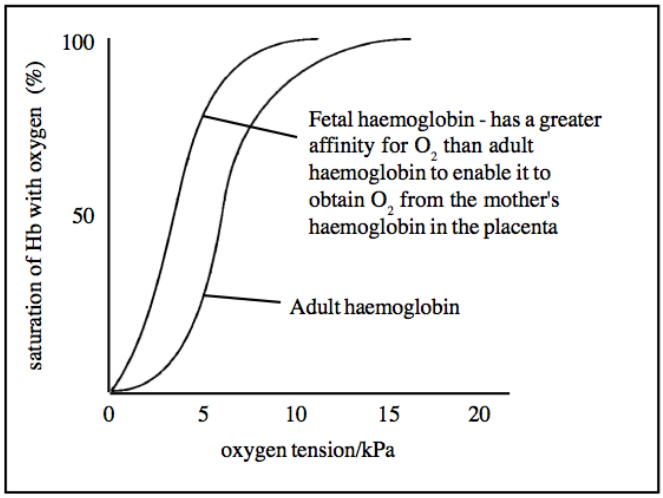
In the alveolar capillaries the equilibria of these reactions is altered. Carbaminohaemoglobin releases its carbon dioxide into the alveoli and the higher oxygen tension dislodges the hydrogen ions from the haem groups. Hydrogen ions react more easily with hydrogencarbonate ions than with chloride ions and so hydrogencarbonate ions diffuse back into the red cell from the plasma in exchange for chloride ions. Carbonic acid then reforms and at once dissociates under the influence of carbonic anhydrase to give water and carbon dioxide. This diffuses along the concentration gradient into the alveolar air and is expired. The blood pH rises no further than pH 7.6.

The effects of other factors on blood gas transport

1. Carbon monoxide tension. This gas is released from car exhausts and from inadequately ventilated gas fires. It competes with oxygen for the haem groups of haemoglobin with which it binds irreversibly, causing death. Haemoglobin in combination with carbon monoxide is called **carboxyhaemoglobin**.

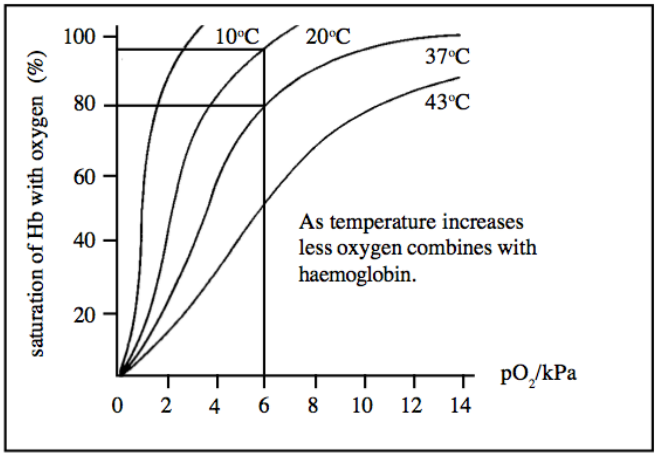
2. Birth. Although a foetus has lungs, it does not use them until the moment of birth. Fetal haemoglobin takes oxygen from mother's haemoglobin across the placenta. Thus fetal haemoglobin must **onload** oxygen at the oxygen tension at which maternal haemoglobin is offloading it. Thus fetal haemoglobin has a greater affinity for oxygen than adult haemoglobin. This can be seen in Figure 3.

Fig 3. ODCs of maternal and fetal haemoglobin



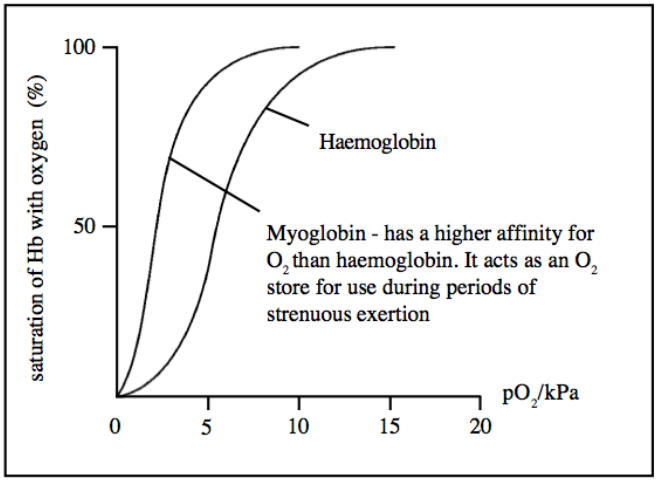
3. Temperature. As temperature increases, less oxygen combines with haemoglobin and the dissociation curve shifts to the right. This can be seen in Fig 4. In other words, as temperature rises, more oxygen is released from haemoglobin. Again, this is exactly what is needed. Heat energy is a product of metabolism. Active tissues such as contracting muscle fibres require large quantities of oxygen, and because of their activity release more acid and heat. These in turn stimulate the haemoglobin to release more oxygen.

Fig 4. The effect of temperature on the oxygen dissociation curves



For example, in tissues which have pO_2 = 6kPa:
At 20°C the Hb would be 97% saturated
At 37°C the Hb would be 80% saturated
The difference - 17% - has been released to the respiring tissues. Clearly, the temperature of mammalian blood does not fluctuate between 20°C and 30°C but this does illustrate the general principle.

Fig 5. Oxygen dissociation curves for haemoglobin and myoglobin



Skeletal muscle also contains its own respiratory pigment, **myoglobin**. This has similar structure and function to haemoglobin and will hold and store oxygen in the muscle until required. Its oxygen dissociation curve lies to the left of that for haemoglobin so that it can onload oxygen at tensions where haemoglobin is releasing it (Fig 5). Myoglobin will only release oxygen at very low partial pressures of oxygen - in other words, it acts as an **oxygen store**.

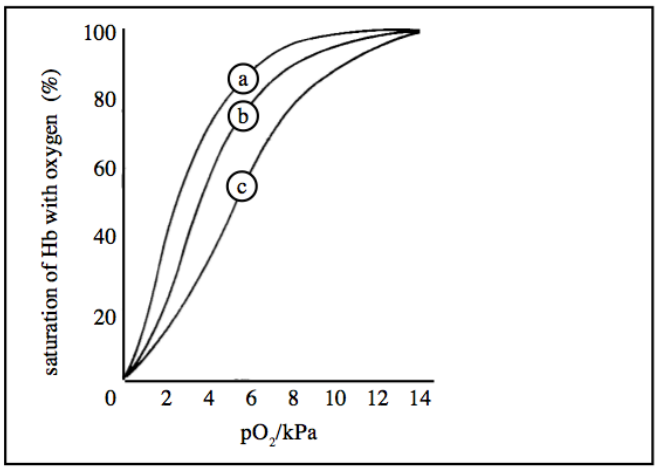
4. Disease. This may cause elevation in the body temperature and thus increase oxygen release to tissues (Fig 4). Anaemia will reduce the quantity of red blood cells and haemoglobin available to transport oxygen. Haemoglobin which is present in sickle cell anaemia has greatly reduced ability to transport oxygen.

5. Ecological factors. Animals which live in permanently reduced oxygen tensions tend to have haemoglobins which will pick up oxygen more readily at such tensions than normal haemoglobin. Thus, the dissociation curves of organisms such as mammalian parasites or mud dwelling worms usually lie to the **left** of the normal curve.

6. Body size. Small animals tend to have higher metabolic rates than large animals and thus their tissues require larger quantities of oxygen. Thus their dissociation curves will lie to the **left** of the normal curve, thus enhancing oxygen uptake and release. Their haemoglobins should however be equally effective at onloading oxygen.

Practice Questions

1. The graph shows the effect of different partial pressures of carbon dioxide on the oxygen dissociation curves.



(a) Which of the curves a, b or c represents the greatest carbon dioxide concentration? (1 mark)
(b) What name is given to the effect shown in the graph? (1 mark)
(c) Explain how this enables respiring tissues to effectively obtain oxygen. (3 marks)
(d) State one other factor which has a similar effect on the oxygen dissociation curve. (1 mark)

Answers

1.
(a) c;
(b) Bohr effect;
(c) Respiring tissues release CO_2;
As CO_2 increases saturation of Hb decreases;
This provides respiring tissues with O_2;
Allowing aerobic respiration to continue; *(any three)*
(d) Temperature;

Acknowledgements;
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